Autonomic Activation During Sleep in Posttraumatic Stress Disorder and Panic: A Mattress Actigraphic Study

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Background: While it has been reported that persons with posttraumatic stress disorder (PTSD) manifest tonic autonomic activation, the literature contains numerous counterexamples. In revisiting the question, this study employed a novel method of mattress actigraphy to unobtrusively estimate heart rate and respiratory sinus arrhythmia over multiple nights of sleep in the home.

Methods: Sleep cardiac autonomic status was estimated in four diagnostic groups, posttraumatic stress disorder, panic disorder, persons comorbid for both conditions, and control subjects. All 59 participants were community-residing nonveterans screened for sleep apnea and periodic leg movement disorder with polysomnography. Heart rate and respiratory sinus arrhythmia were calculated from the kinetocardiogram signal measured via accelerometers embedded in a mattress topper. Times in bed and asleep were also estimated. Per participant data were obtained from a median of 12 nights.

Results: Both posttraumatic stress disorder and posttraumatic stress disorder/panic disorder comorbid groups exhibited significantly higher heart rates and lower respiratory sinus arrhythmia magnitudes than panic disorder participants and control subjects. Panic disorder participants were indistinguishable from control subjects. The PTSD-only group exhibited longer times in bed and longer times presumably asleep than the other three groups.

Conclusions: In this study, posttraumatic stress disorder, but not panic disorder, was associated with altered cardiac autonomic status during sleep. Among participants meeting criteria for PTSD alone, autonomic activation co-occurred with prolongation of actigraphic sleep.

Key Words: Autonomic status, panic disorder, posttraumatic stress disorder, sleep

The literature on basal autonomic status in posttraumatic stress disorder (PTSD) contains numerous inconsistencies. Lately, this issue has acquired additional significance with the emergence of an association between basal heart rate (HR) and metabolic syndrome (1–3). In the laboratory, phasically elevated HR is reliably observed in persons with PTSD as they anticipate re-exposure to trauma reminders (4–6). Heart rate is also elevated in the acute aftermath of trauma in persons who go on to develop PTSD (7–9). Whether this heralds a persistent elevation in those same persons is unknown, as longitudinal studies have yet to be performed. Three laboratory studies in combat veterans failing to observe HR elevations all informed participants they would not be exposed to trauma reminders but instead to generic stressors such as orthostatic challenge, cold pressure, and a mock job interview (10–12).

Two approaches to addressing this question deserve special attention. The first, measurement during sleep, appears to provide an opportunity to assess tonic autonomic activation largely free of influences of affect and cognition. As well, sleep has been shown to be independently relevant to appetite regulation, obesity, and diabetes, all associates of metabolic syndrome (13). Woodward *et al.* (14) recorded continuous electrocardiogram (ECG) in 56 unmedicated male combat veterans and 14 mixed-trauma, age- and gender-matched control subjects during laboratory sleep studies employing conventional polysomnography (PSG). Heart rate estimates were obtained from PSG-verified sleep and per night HRs averaged over two to four postadaptational nights. They observed no effect of PTSD diagnosis on sleep HR and no association between HR and hyperarousal (D-Criterion) scores obtained using the Clinician-Administered PTSD Scale (CAPS) (15). The D-criterion scores were, instead, associated with electroencephalogram (EEG) power in higher frequencies. An important qualification of this result is the low rate of emergence, in the laboratory, of a key symptom of PTSD-related sleep disturbance, trauma-related nightmares (16). A second approach, ambulatory measurement, would appear to offer increased reliability and validity. Beckham *et al.* (17) tested 117 male combat veterans with and without PTSD using ambulatory blood pressure (BP) monitoring. An analysis accounting for self-reported activity level found PTSD to be associated with a 5 beat-per-minute (BPM) increase in basal HR. A smaller study by Buckley *et al.* (18), also adjusting for body mass index, smoking status, and ethnicity, found that basal HR was 6.63 BPM higher in PTSD-positive participants than in control subjects. While both the Beckham *et al.* (17) and Buckley *et al.* (18) studies included the sleep period, neither could verify sleep. In addition, in ambulatory BP monitoring, HR is measured solely during the cuff inflation-deflation cycle; hence, HR estimates are unavoidably confounded with responses to this mildly aversive stimulus. While these generic stimuli might not be expected to induce exaggerated responses in PTSD, it is not clear that this argument extends to the sleep periods, which constituted a substantial fraction of measurement periods in both studies. In normal subjects, BP cuff inflation during sleep often leads to awakenings (19), which are typically associated with elevations of HR and BP (20).

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The current study sought to combine virtues of both ambulatory and sleep-based measurement by measuring HR and respiratory sinus arrhythmia (RSA) during the sleep period for an extended period in the home. It employed a novel sleep assessment method, mattress actigraphy, which transduces large and small sleeper movements using accelerometers embedded in a mattress topper. These small movements include the kinetocardiogram (KCG), which, for movement-free periods, closely tracks the ECG (21). Because mattress actigraphy employs no body surface sensors, in-home recordings can be continued indefinitely. In the current study, a median of 12 nights of recording was obtained from participants. Conventional actigraphic sleep variables were also calculated. In addition, this study employed a sample including participants meeting criteria for PTSD, panic disorder (PD), and both PTSD and PD, who were otherwise free of Axis I psychopathology (other than dysthymia). As such, this study represents the first direct comparison of sleep in PTSD with PD, two anxiety spectrum disorders sharing dysphoric episodic sympathetic activations and subjectively poor sleep (22).

Methods and Materials

Participants

This research was performed under the auspices of the Stanford/Veterans Affairs (VA) Palo Alto Human Research Protection Program. Written informed consent was obtained from all participants passing telephone screening. If present, a sleep partner had also to agree to actigraphic recording during the in-home portion of the study. Participants were recruited from the community using radio and newspaper advertisements emphasizing disturbances of sleep due to distressing experiences, fear and anxiety, and/or nightmares and nocturnal panic attacks. The recruitment of participants denying subjective sleep complaints relied principally on personal contacts between study participants and study staff and their respective social networks. Telephone screening excluded callers if they reported current medical illness, histories of central nervous system disease or injury, a Multivariate Apnea Prediction Index (MAPI) (23) greater than .5, or a previously diagnosed medical sleep disorder (e.g., obstructive sleep apnea or periodic limb movement disorder). Persons were also excluded if they were currently abusing alcohol or other psychotropic substances or were unwilling to discontinue hypnotic medications. Provisional diagnoses were made during telephone screening requiring from 15 to 60 minutes. Participants passing screening traveled to the research setting and underwent structured interviews. Diagnoses of PTSD and PD were based on the CAPS and the PD section of the Structured Clinical Interview for the DSM-IV (SCID) (24), respectively. Trauma histories were determined prior to administration of the CAPS using the Life Events Checklist (25) and Life Events Follow-Up Interview (D.G. Kaloupek and C. Kutter, unpublished data, 1999). Typical of community samples, index traumas were mostly single incidents such as motor vehicle accidents, criminal victimizations, and exposures related to the 1989 Loma Prieta earthquake. Screening of other Axis I psychopathology was confirmed using the Mini-International Neuropsychiatric Interview (MINI) (26). Eight participants diagnosed with dysthymic disorder were retained. Participants were administered the Beck Depression Inventory-II (BDI-II) (27), the Beck Anxiety Inventory (BAI) (28), and the Pittsburgh Sleep Quality Index (PSQI) (29). The latter included the PTSD addendum comprising 10 questions focusing on nocturnal arousals, nightmares, and related anxiety.

Seventeen participants meeting screening and diagnostic criteria declined to return for a screening PSG. Ten participants who underwent PSG had apnea/hypopnea indices (AHIs) greater than 10 events per hour. Three participants were excluded due to periodic limb movement arousal indices (PLMAIs) greater than 20 events per hour (AHIs and PLMAIs were manually scored using the LifeShirt (VivoMetrics, Ventura, California) records and PSG records, respectively). Ten participants who passed the screening PSG declined to undergo in-home recording. Among those recorded at home, seven were excluded due to equipment failure. While many potential participants were lost due to sleep medical conditions, voluntary discontinuation, or equipment failure, noncompleters were evenly distributed over diagnoses (14 PD, 14 PTSD, 13 PTSD+PD, 8 control subjects). Completing participants were paid $300. Noncompleters received prorated payments. Participants were asked to maintain their nonhypnotic medications. Rates of psychotropic medication use differed over diagnostic groups [control subjects, 0%; PD, 18%; PTSD, 27%; and PTSD+PD, 45%; $\chi^2(3) = 7.87$, $p < .05$]. There were no associations between group and specific classes of medication: selective serotonin reuptake inhibitor (SSRI) antidepressants [$\chi^2(3) = 2.68$, ns, 14% of total sample]; non-SSRI antidepressants [$\chi^2(3) = 4.50$, ns, 8% of sample]; anxiolytic agents [$\chi^2(3) = 5.97$, ns, 5% of sample]. No participants were taking stimulants or beta-blockers. Three tested participants reported having prescriptions for hypnotic medications, which they agreed to discontinue.

Procedures

Participants came to the study site in the afternoon to complete diagnostic interviews and self-report psychometrics. After dinner, they came to the sleep laboratory to prepare for the screening PSG. The PSG montage included EEG (Cz and Pz referenced to linked ears), electro-oculogram (EOG) (vertical and horizontal), submental electromyogram (EMG), bilateral anterior tibialis EMG, and oral/nasal airflow (thermistor). Electrocardiogram and respiratory effort (RESP, thoracic and abdominal bands, inductive plethysmography) were recorded via a VivoMetrics LifeShirt system. After completion of a presleep startle protocol, participants went to sleep ad libitum.

Home sleep recording involved installation of the mattress actigraphy system and setting up the participant for a single night of concurrent ambulatory PSG. Ambulatory PSG employed EEG (Cz and Pz referenced to linked ears), EOG (horizontal only), submental EMG, and ECG. Participants were also fitted with an ankle actigraph (Octagonal Sleep Watch, Ambulatory Monitoring, Inc., Ardsley, New York) to be worn while in bed for the duration of the home study. Participants denying any nocturnal paroxysmal symptoms were recorded for approximately 1 week. Participants reporting such symptoms were recorded for up to a month. The following results are based on mattress actigraphy data from all home nights, excluding the night of concurrent ambulatory PSG.

Mattress actigraphy was recorded by four sensitive, low-noise, direct current (DC) accelerometers (Silicon Designs 2010, Silicon Designs, Inc., Issaquah, Washington) embedded in a mattress topper that was placed on top of the participant's regular mattress. The topper was composed of a 1-inch foam pad encased in bacteriostatic ticking. The accelerometers were suspended in spandex "trampolines" over 3-inch diameter holes in the underlying foam to promote compliance under load. The net effect was not unlike a pillow-top mattress of which most participants spoke favorably, none discontinuing on the basis of discomfort. The accelerometers were connected to a 12-volt

Table 1. Means and Standard Deviations of Indices of Medical Sleep Disorder and Psychiatric Severity Across Groups

	Control Subjects $n = 13$		Panic Disorder $n = 13$		PTSD $n = 22$		PTSD+Panic Disorder $n = 11$		Effect Size of Diagnosis (Partial h^2) Where $\alpha < .05$
	M	SD	M	SD	M	SD	M	SD	
Age	39.6	10.8	42.1	11.0	42.2	12.8	42.0	13.9	
BMI	22.1	4.8	25.5	4.9	26.2	5.7	26.6	6.2	
MAPI	.1	.1	.2	.1	.2	.2	.2	0.2	
AHI	3.0	2.6	2.6	2.5	2.5	1.8	2.7	2.0	
PLMAI	.7	3.1	2.7	3.2	.9	3.7	1.7	4.1	
Education	16.1	3.3	14.7	3.5	14.7	4.3	13.5	4.3	
Work Hours/Week	28.5	18.5	38.8	20.1	27.6	24.4	22.9	24.2	
BDI-II	.4	8.4	10.2	8.6	14.2	10.9	20.4	10.8	.381
BAI	1.2	9.8	15.8	10.1	10.8	12.8	26.7	12.7	.393
PSQI	8.0	2.2	9.4	2.3	11.5	2.9	11.4	2.9	.273
PSQI PTSD Addendum	7.5	3.2	9.9	3.3	13.3	4.1	16.2	4.1	.454

AHI, apnea/hypopnea indices; BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory-II; BMI, body mass index; MAPI, Multivariate Apnea Prediction Index; PLMAI, periodic limb movement arousal indices; PSQI, Pittsburgh Sleep Quality Index; PTSD, posttraumatic stress disorder.

medical grade power supply (Condor MLL 250, Mouser Electronics, Mansfield, Texas) and to a data acquisition card (Kiethley KMPCI 3807, Keithley Instruments, Inc., Cleveland, Ohio) that sampled the movement data at 600 Hz with 16 bits of amplitude resolution. Extraction of HR and RSA from the actigraphic record began with visual inspection and determination of the onset and offset of the intended sleep period (ISP) determined using all available data, including ambient light and sound. Automated computer-based processing began with the identification of epochs of stable body position. Within these epochs, the sensor supplying the KCG signal with the highest signal-to-noise ratio was identified. Extraction of KCG beats began with determination of the canonical (median) KCG ensemble for each epoch. These were then used as templates to identify beats as locations of high-cross correlation with the raw data. At each stage, strict artifact exclusion criteria were applied with the result that per-night estimates were based on approximately 3 hours of recording, on average. The aggregate time producing low-artifact KCG beat series, here labeled "KCGtime," was co-determined by time in bed and by typical KCG signal quality. The latter, in turn, was determined by the presence/absence of body movements contaminating the KCG and by body position in relation to the sensors (prone vs. supine vs. lateral), which was not recorded. As with all actigraphy, epochs of low movement were used to estimate sleep versus wake but could not provide direct information regarding sleep stage. Additional details of the estimation of HR and RSA from the KCG have been published elsewhere (21).

Twenty participants had sleeping partners for some or all nights. Participant/partner pairs were issued a double topper that included a single sensor under the thorax of the partner. While participant KCG dominated the signals at sensors under his or her own thorax, an opportunity for signal "bleed" arose when sleeping was asynchronous. All participant/partner HR time series were reviewed for evidence of cross-sleeper artifact. This effort was facilitated by the concentration of such artifacts at the beginning, and end, of nights, the availability of nightly records of the presence/absence of a partner, and the fact that sleeper pairs typically had distinct baseline HRs. Substantial cross-sleeper artifact was found in 21 nights. These were excluded and per-participant across-night median HR and RSA values were recalculated. Postexclusion, the mean deviation was −.079 BPM, and no per-participant median diverged from the original value by more than .73 BPM.

Differences between diagnostic groups were tested with univariate analyses of variance (ANOVAs) followed by Fisher's least significant difference (LSD). Relations among continuous variables were assessed using simple and partial correlation and multiple regression (30).

Results

Demographic, sleep-medical, and psychometric data characterizing the final sample of 59 participants are summarized in Table 1. The BDI-II exhibited a moderate effect of group [$F(3,50) = 10.3$, $p < .001$, partial $\eta^2 = .381$] and a modest effect of gender [$F(1,50) = 4.7$, $p < .05$, partial $\eta^2 = .087$] (BDI-II, BAI, and PSQI scores were missing for one PTSD participant.) Control subjects endorsed very little depressive mentation. Among the patient groups, both PD participants (Fisher's LSD: $p < .001$) and PTSD participants (Fisher's LSD: $p < .01$) endorsed significantly less depressive mentation than PTSD+PD participants. Female participants endorsed more than male participants. The BAI exhibited a moderate effect of group [$F(3,50) = 10.8$, $p < .001$, partial $\eta^2 = .393$] and a group by gender interaction [$F(3,50) = 3.6$, $p < .05$, partial $\eta^2 = .177$]. Again, control subjects endorsed little anxious mentation relative to the anxiety disorder groups. Among the latter, PTSD+PD participants endorsed significantly more than PTSD participants (Fisher's LSD: $p < .001$). The group by gender interaction originated in the observation that female PD participants endorsed significantly more anxious mentation than male PD participants [$t(11) = 2.74$, $p < .05$], whereas at other levels of the group factor there were no gender differences. The Pittsburgh Sleep Quality Index exhibited a large effect of group [$F(3,50) = 6.3$, $p < .001$, partial $\eta^2 = .273$]. Again, control subjects reported less sleep complaint than the anxiety disorder groups, though control subjects' PSQI scores were in the low clinical range. Among anxiety disorder groups, PTSD participants reported significantly more sleep complaint than PD participants (Fisher's LSD: $p < .05$). The PTSD addendum of the PSQI also exhibited a large effect of group [$F(3,50) = 13.9$, $p < .001$, partial $\eta^2 = .454$], with both PTSD participants (Fisher's LSD: $p < .01$) and PTSD+PD participants (Fisher's LSD: $p < .001$) endorsing significantly more PTSD-related sleep symptomology than PD participants. Eleven of 13 control subjects and 5 of 13 PD participants denied any history of trauma. Among anxiety disorder participants endorsing a trauma history, the number of different trauma types reported was associated with diagnosis

Table 2. Least-Squares Means (Controlled for Gender) and Standard Deviations of Mattress Actigraphic Indices of Nocturnal Quiescence and Autonomic Status

	Control Subjects $n = 13$		Panic Disorder $n = 13$		PTSD $n = 22$		PTSD+Panic Disorder $n = 11$		Effect Size of Diagnosis (Partial h^2) Where $\alpha < .05$
	M	SD	M	SD	M	SD	M	SD	
Actigraphy Nights	6.7	4.3	12.0	4.4	14.6	5.1	10.9	5.5	.346
ISP Minutes	472.5	61.5	436.9	58.6	504.6	68.1	435.1	83.5	.194
KCG Minutes	224.4	49.1	195.4	50.3	240.5	58.4	179.9	63.4	.156
HR	61.2	7.7	61.3	8.0	66.6	9.2	69.8	10.0	.148
RSA Magnitude	.25	.08	.31	.09	.21	.10	.21	.11	.177

HR, heart rate; ISP, intended sleep period; KCG, kinetocardiogram; PTSD, posttraumatic stress disorder; RSA, respiratory sinus arrhythmia.

[$F(2,34) = 5.65$, $p < .01$], being significantly elevated in those meeting criteria for PTSD (Fisher's LSD: $p < .05$) and PTSD+PD (Fisher's LSD: $p < .01$) relative to PD alone. The number of different trauma types reported was not associated with gender ($F < 1$). The anxiety disorder groups did not differ in terms of age at first trauma ($F < 1$).

Diagnostic groups were closely matched on physical and medical characteristics associated with effects on sleep other than those under consideration, including age, body mass index (BMI), apnea-hypopnea indices, and periodic limb movement arousal indices. Control subjects had slightly lower BMIs than the PTSD participants (Fisher's LSD: $p < .05$) and PTSD+PD (Fisher's LSD: $p < .05$). Female participants had lower MAPI scores than male participants [$F(1,51) = 5.5$, $p < .05$, partial $\eta^2 = .098$]. Neither diagnosis nor gender was associated with differences in years of education or hours worked per week.

Additional characteristics of the mattress actigraphy sleep sample can be found in Table 2. Because control subjects all denied experiencing any nocturnal paroxysmal events, they were recorded for fewer nights, on average, than the patient groups [$F(3,51) = 8.3$, $p < .001$, partial $\eta^2 = 0.327$]. Posttraumatic stress disorder participants were recorded on significantly more nights than PD participants (Fisher's LSD: $p < .05$). The average ISP (calculated over all nights providing interpretable ISPs and without regard to the quality of KCG data) exhibited a main effect of diagnosis [$F(3,51) = 3.43$, $p < .05$, partial $\eta^2 = .194$]. Surprisingly, PTSD participants exhibited significantly longer in-bed periods than either PD participants (Fisher's LSD: $p < .001$) or PTSD+PD participants (Fisher's LSD: < 0.01). Mean KCGtime values are presented in Table 2. The KCGtime also exhibited a main effect of diagnosis [$F(3,51) = 3.33$, $p < .05$, partial $\eta^2 = .164$]. As before, PTSD participants exhibited raw KCGtimes that were significantly longer than both PD participants (Fisher's LSD: $p < .01$) and PTSD+PD participants (Fisher's LSD: $p < .001$) but not longer than control subjects. The KCGtimes of the PTSD+PD group were also shorter than those of control subjects (Fisher's LSD: $p < .05$). The KCGtime exhibited an effect of gender [$F(1,51) = 4.43$, $p < .05$, partial $\eta^2 = .080$], being on average 30 minutes shorter in women. When KCGtime was reanalyzed as a percentage of the ISP, there was no main effect of diagnosis ($F < 1$) but again an effect of gender [$F(1,51) = 8.30$, $p < .01$, partial $\eta^2 = .140$], with male participants exhibiting more KCGtime than female participants. In male participants, KCG-based HR and RSA were obtained from approximately 51% of the intended sleep period, in female participants, 41%. Typical total sleep HR and RSA samples were approximately 40 hours.

Sleep HR exhibited a main effect of diagnosis [$F(3,51) = 2.89$, $p < .05$, partial $\eta^2 = .145$]. Posttraumatic stress disorder participants' sleep HRs were higher than those of control subjects (Fisher's LSD: $p < .05$), as were those of PTSD+PD participants (Fisher's LSD: $p < .05$). Heart rates of control subjects and PD participants did not differ (Figure 1). There was no effect of gender and no diagnosis × gender interaction (Fs < 1). Sleep RSA magnitude also exhibited a main effect of diagnosis [$F(3,51) = 3.55$, $p < .05$, partial $\eta^2 = .173$]. Panic disorder participants exhibited higher sleep RSA magnitude than PTSD (Fisher's LSD: $p < .001$) and PTSD+PD participants (Fisher's LSD: $p < .05$) (Figure 1). Covariation for age, AHI, BMI, PLMAI, and KCGtime had no impact on the between-group results for sleep HR and RSA.

Neither BDI scores, BAI scores, nor CAPS severity scores (in PTSD and PTSD+PD participants) were correlated with sleep HR or RSA magnitude. Beck Anxiety Inventory scores were inversely correlated with KCGtime over all participants [$r(57) = -.341$, $p < .01$] and after excluding control subjects [$r(43) = -.341$, $p < .05$]. Sleep HRs correlated positively [$r(56) = .332$, $p < .05$] and sleep RSA magnitudes negatively [$r(56) = -.333$, $p < .05$] with PSQI total scores (Figure 2). Sleep HR was also correlated with the PSQI PTSD addendum score [$r(56) = .406$, $p < .01$]. This pattern was preserved when control subjects were excluded. The rela-

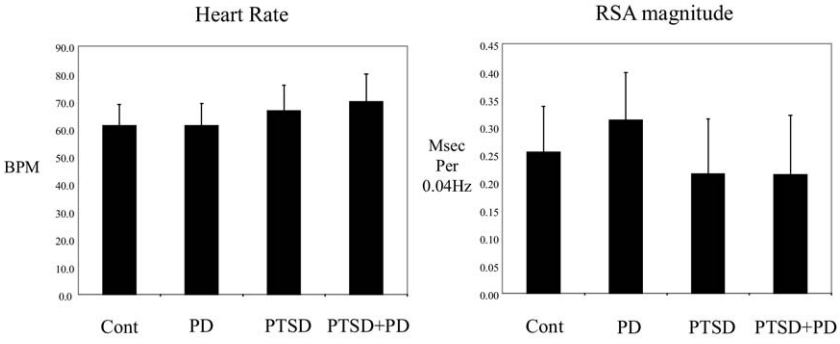

Figure 1. Bar graphs plotting least-squares means and standard deviations of all-night heart rates and respiratory sinus arrhythmia magnitudes for each participant group. Cont, control subjects; PD, panic disorder; PTSD, posttraumatic stress disorder; PTSD+PD, subjects comorbid for both posttraumatic stress disorder and panic disorder; RSA, respiratory sinus arrhythmia.

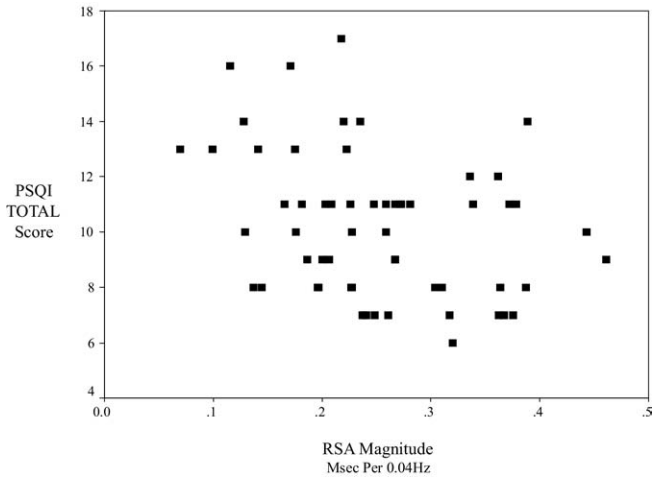

Figure 2. Scatterplot of PSQI total score and all-night respiratory sinus arrhythmia magnitudes across all participants. PSQI, Pittsburgh Sleep Quality Index; RSA, respiratory sinus arrhythmia.

tion between PSQI scores and RSA magnitudes was re-evaluated controlling for age, BAI, and BDI scores. The intent of this analysis was to isolate variance in PSQI not associated with aging and waking dysphoria. Significant increases in PSQI variance explained were evident at all steps. In the final model, only BAI and sleep RSA magnitude retained beta weights significantly different from zero (BAI: $\beta = .413$, $t = 3.05$, $p < .01$; RSA: $\beta = -.284$, $t = 2.39$, $p < .05$). The model accounted for 37% of variance in PSQI scores in the sample composed of both anxiety disorder participants and control subjects [adjusted $R^2 = .371$, $F_{\text{regression}}(4,53) = 9.48$, $p < .001$]. Restricting the analyses to anxiety disorder participants produced a similar result [BAI: $\beta = .339$, $t = 2.28$, $p < .05$; RSA: $\beta = -.405$, $t = 2.74$, $p < .01$; adjusted $R^2 = .247$, $F_{\text{regression}}(4,40) = 4.61$, $p < .01$]. The waking disturbance score of the PSQI (not incorporated into the PSQI score itself) was positively correlated with sleep HR [$r(56) = .337$, $p < .01$] and negatively correlated with KCGtime [$r(56) = -.324$, $p < .05$]. The latter correlations remained significant after controlling for age, BDI, BAI, and PSQI total score in the whole sample [HR: $r(52) = .381$, $p < .01$; KCGtime: $r(52) = -.275$, $p < .05$] and in the anxiety disorder participants [HR: $r(39) = .407$, $p < .01$; KCGtime: $r(39) = -.349$, $p < .05$].

Discussion

Consistent with the findings of both Beckham *et al.* (17) and Buckley *et al.* (18), sleep HR in PTSD and PTSD+PD participants was significantly elevated relative to control subjects. For PTSD participants, the magnitude of HR elevation was very similar to observations made by those investigators. For PTSD+PD participants, the elevation was over 8 BPM. The pattern of results among PTSD, PD, and control subjects closely approximated the observations of Blechert *et al.* (31), who found baseline HR elevation in PTSD but not PD in a community sample. Sleep RSA magnitude presented a corresponding pattern, with PTSD and PTSD+PD participants exhibiting lower magnitudes, although here the significant contrasts were with PD participants. In waking, Blechert *et al.* (31) observed RSA power to be lower in PTSD than in PD and not different between PD and control subjects; however, in that study, PTSD participants also exhibited significantly lower RSA power than control subjects. The association of PTSD with elevated sleep HR provides an intriguing context for further tests of prazosin to treat sleep disturbances in this disorder. While prazosin reduces nightmares and improves subjective sleep in PTSD (32,33), it does not, at least when administered to hypertensive men, lower heart rate (34).

An important limitation of this study is the absence of a subgroup with histories of trauma that did not manifest PTSD. Hence, trauma per se cannot be excluded as the cause of excess autonomic activation in the PTSD and PTSD+PD groups. We also note that multiple factors favored low symptom severity among the anxiety disorder persons studied. These include the intensity of the study, the use of a community sample, and the exclusion of additional Axis I psychopathology. Commensurate with this are a preponderance of single-incident trauma histories among PTSD participants and a low rate of psychotropic use overall (26%). That such a low-severity sample manifested significant associations between PTSD and altered sleep cardiac autonomic status, while chronic severe combat-related PTSD inpatient male subjects studied in our laboratory have not, is intriguing. Extended in-home studies of combat veterans may resolve this apparent inconsistency.

We suspect that contrasting persons with PD, PTSD, and PTSD+PD promoted the creation of diagnostically "clean" groups. From this perspective, it is noteworthy that, when considered simultaneously in terms of sleep cardiac autonomic status and actigraphic sleep/wake findings, these groups are not metrically related. Panic disorder participants appeared essentially normal in both domains. Findings in comorbid participants, though broadly consistent with the exaggeration of subjective sleep complaints reported by Leskin *et al.* (35), could not be extrapolated from those with PTSD and PD. In a similar vein, the actigraphic sleep profiles of PD, PTSD, and PTSD+PD groups fell into distinct risk categories in relation to metabolic syndrome (13). Panic disorder participants exhibited no evidence of elevated risk from sleep restriction or tonic sympathetic activation. The PTSD+PD participants exhibited elevated risk due to both sleep restriction and sympathetic activation. The PTSD-only patients presented contradictory indications, combining tonically elevated sympathetic tone with extended sleep periods. Careful attention to distinctions among PD, PTSD, and PTSD+PD phenotypes may prove productive in future studies of associations between metabolic syndrome and psychiatric status. Finally, PTSD-only participants spent more time in bed and more time immobile, yet still slept worse to the extent that autonomic quiescence during sleep has positive health implications. If this paradoxical pattern can be replicated, we may then ask whether it represents an adaptive strategy for achieving the biological goals of sleep while retaining the capacity for rapid awakening.

Actigraphy infers sleep from immobility; however, immobility can be measured with varying precision and may mean different things in different diagnostic groups (21,36). Analyses are now underway in our laboratory to evaluate the relative capacities of the different immobility indices obtainable from mattress actigraphy to predict PSG-defined sleep. Among these, KCGtime is a very strict index because it excludes any epoch containing movement sufficient to introduce artifact into the KCG time series. The observed relationships between KCGtime and the waking disturbance subscore of the PSQI provide preliminary evidence that quantifying in-bed time devoid of even the smallest and briefest of movements may prove a productive extension of the actigraphic measurement of sleep.

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Dr. Woodward is the inventor of the SensorBed. The patent (US 6,485,441) is co-assigned to the Department of Veterans Affairs and to Leland Stanford University. The SensorBed has not been licensed for commercialization. In the event of such licensure, Dr. Woodward could benefit indirectly in his official capacity as a federal employee, as one third of any royalties would be paid into the general fund of the Veterans Affairs Palo Alto Health Care System and from there could be assigned to Dr. Woodward for research-related expenditures. No royalty earnings would accrue to Dr. Woodward were he to separate from the Department of Veterans Affairs; however, he could profit financially as a private citizen through personally licensing and commercializing the SensorBed in the event that profits were realized.

All other authors reported no biomedical financial interests or potential conflicts of interest.

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